Clinical Feature:
Side Effects of Anabolic Steroids
—Negah Rassouli, MD
—Don H. Catlin, MD
—Fred H. Faas, MD

In this issue
• MWLA 2009 Preview • Case Studies and Practical Pearls on Diabetes • CVD Risk Assessment
From the
President

VERA BITTNER, MD, MSPH
NLA President
Professor of Medicine
Division of Cardiovascular Disease
University of Alabama at Birmingham
Birmingham, AL
Diplomate, American Board of Clinical Lipidology

NLA —-2010: Where are we going?

Professional Education Programs
As has been the case throughout the existence of the NLA, professional education remains the major focus of the organization. We will continue to offer both the Lipid Management Training Course and the Masters Course in conjunction with regional and national meetings. Under the leadership of Dr. Mary McGowan, who leads the LMTC effort, and Drs. Michael Davidson and Peter Toth, who lead the Masters Effort, the curriculum for both courses is being reviewed continuously and slides and other course materials are being updated on an ongoing basis to stay current with the rapidly evolving literature. The NLA Self-Assessment Programs (now available on the Web), the Clinical Lipid Management Self-Assessment Programs, CME meetings on a variety of topics, and the Virtual Lipid Clinic round out the teaching portfolio.

Past symposia in conjunction with AHA and ACC meetings have been very well received. At AHA 2009, NLA will present a symposium in close collaboration with the American Society of Hypertension and the American Society of Preventive Cardiology which will address hot topics in dyslipidemia, hypertension, diabetes and obesity management. You won’t want to miss this event—be sure to mark your calendars for Saturday, November 14, and keep an eye on www.lipid.org for additional details. For those of you who cannot attend, content will be made available on Medscape.

Publications
The Lipid Spin has greatly thrived under Drs. Maria Lopez-Virella’s and Ron Goldberg’s able leadership. As they have served as editors for several years, as of this issue they are relinquishing their duties to Drs. James Underberg and Robert Wild, who are members of the Communications Committee and volunteered for this duty. The responsibility for providing content rotates from chapter to chapter. Please contact your chapter leadership, if you are interested in contributing articles, clinical vignettes or other content. For those of you who are interested in getting more involved in the organization, this is a wonderful opportunity to do so.

The Journal of Clinical Lipidology is growing in stature under Dr. W. Virgil Brown’s guidance. The journal is now in its 3rd year and publishes original articles, reviews
and case studies. Instructions for authors are available at ees.elsevier.com/jclinlipid. We encourage all NLA members who publish to please consider the Journal of Clinical Lipidology, first.

International Initiative
Dr. Virgil Brown and the administrative staff have been hard at work on the international outreach program. We now have an official name for this effort: the International Federation of Clinical Lipidology. The major goal of this worldwide federation of independent clinical lipidology associations will be to share ideas and programs designed to improve professional services in the area of Clinical Lipidology. As a first step, we are developing plans to run the Masters Course in different geographic regions jointly with the regional Clinical Lipidology leadership. This will require additional funding and finding partners willing to join us with financial support is critical to the success of this exciting initiative.

Stay tuned—more details on this are to come in future issues of the Lipid Spin.

Lipidologists in Training – We Want You to Get Involved!
In-Training Members have been added to 3 of the 5 regional boards and will be added shortly to the remaining 2 chapters. The regional and national meetings provide an excellent forum to present your research data at the poster competition, get up to date and in depth education on a variety of clinical lipidology topics, and to network with experienced clinical lipidologists in practice and in academic settings. Most of you are already familiar with the potential of the Web 2.0 framework at Lipid.org and you’ll find that the NLA Community site is equally easy to use—take advantage of it and create your own discussion groups and forums. You can always contact Karen Kent at the NLA if you need assistance in accessing the website resources available to you (kkent@lipid.org).

continued on page 24
Striking Lipoprotein Changes and Liver Toxicity Induced by Over-The-Counter Androgen Supplements

INTRODUCTION
Androgenic Anabolic Steroids (AAS) have been associated with a wide range of adverse effects. Some of these products can be easily obtained over the internet, where they are marketed as “dietary supplements” and “pro hormones.” Consumers are not always aware of the potential side effects.1

Here, we report various side effects of two over-the-counter (OTC) bodybuilding supplements, Superdrol (methasteron) and Orastan-E (prostanozol), in a young, previously healthy individual.

CASE PRESENTATION
A 28 year-old previously healthy white male presented with a two-week history of nausea, jaundice, pruritis and dark urine. Two months prior to the onset of his symptoms, he had started using the OTC bodybuilding supplements Superdrol (methasteron) and Orastan-E (prostanozol) at daily doses of 40 mg and 50 mg, respectively. Further history revealed that in the few weeks prior to admission, he had noticed decreased sexual desire and difficulty in maintaining an erection. He had been smoking one pack of cigarettes daily for 10 years but he denied using alcohol or illicit drugs. Family history was negative for liver disease or lipid abnormalities. On physical examination, he had an athletic appearance with excoriations throughout the skin. The sclerae were icteric. There was mild right upper quadrant abdominal tenderness. The liver was not enlarged. Laboratory studies (Table 1) revealed an elevated bilirubin and mild elevation of serum transaminases. Extensive work up for the etiology of his jaundice was negative. While prior to using the supplements his lipid profile was normal, at presentation in September 2005, the total cholesterol was

Correspondence:
Fred H Faas MD
Central Arkansas Veterans Healthcare System
4300 West 7th St., Mail Slot 111J
Little Rock, AR, United States, 72205
501-257-5766
E-mail: faasfredh@uams.edu

Figure 1: Chemical structures of testosterone, methasteron, stanozolol and Prostanozol
439 mg/dL, triglycerides 342 mg/dL, high-density lipoprotein cholesterol (HDL-C) 9 mg/dL, and direct low-density lipoprotein cholesterol (LDL-C) 354 mg/dL. Three days later, the HDL-C reached a nadir of 4 mg/dL. His serum testosterone, follicle-stimulating hormone (FSH) and luteinizing hormone (LH) levels were also low. The jaundice, hypogonadism and lipid profiles abnormalities were attributed to his AAS abuse. Several weeks after discontinuation of AAS, the serum testosterone returned to normal. Nevertheless, his libido, pruritis and liver function tests remained abnormal and serum lipids were only slightly improved. A liver biopsy was performed showing pure canalicular cholestasis consistent with an adverse drug reaction. Three months later, the lipid profile returned to baseline with an HDL-C of 39 mg/dL and LDL-C of 168 mg/dL. Liver function tests also normalized. After recovery, the patient provided the investigators with samples of the two supplements. These were analyzed by one of the authors (D.C.). Superdrol contained methasteron and Orastan-E contained 3 peaks on Liquid Chromatography-Mass Spectrometry (LC/MS) analysis, each with a molecular weight corresponding to that of prostanozol. Further studies are needed to establish the exact molecular identity of each peak.

**Discussion**

New “designer steroids” such as prostanozol and methasteron have been available in nutritional supplements markets over the Internet for the last few years and are being advertised as products with “minimal side effects.” While both of these products are on the 2008 prohibited list by the World Anti-Doping Agency (WADA), their legal status is not clear. According to the Anabolic Steroid Control Act (ASCA) of 2004, the sale of anabolic steroid as nutritional supplements is prohibited in the US; however, these products are not on the list of banned steroids. For reference, the chemical structures of Superdrol and Prostanozol with their relation to testosterone and stanozolol (synthetic anabolic steroid derived from testosterone) are shown in Figure 1.

Various side effects have been reported with the use of AAS. A review by Glazer showed that AAS decreased HDL-C levels (40–70%), while it increased LDL-C concentration by an average of 36% (11%–100%). The responsible mechanism is not fully understood; however, it is suggested that oral forms of 17 α-alkylated steroids stimulate hepatic triglyceride lipase, which reduces serum HDL-C. The effect of AAS on serum LDL-C levels is variable, with reports of increase, decrease and no change in LDL-C levels. Relevant to the present report, in one study of male weight lifters, oral administration of stanozolol led to a 29% increase in LDL-C and a 35% increase in apoprotein B levels, whereas intramuscular testosterone treatment caused a 16% decrease in serum LDL-C. Our patient presented with an 87% decrease in HDL-C and a 110% increase in LDL-C levels. These alterations in lipid profiles are more dramatic than any previously reported with AAS use.

It has been suggested that the magnitude of AAS-induced lipoprotein changes are dose dependent and are more severe in poly-drug regimens. This may explain the striking changes in the lipoprotein profile in our patient. Complete recovery from AAS induced lipoprotein changes is more dependent on duration rather than the dosage of AAS. Fortunately, in our

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**Table 1: Patient laboratory results**

<table>
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<tr>
<th></th>
<th>4/25/05</th>
<th>9/22/05</th>
<th>9/25/05</th>
<th>10/24/05</th>
<th>11/7/05</th>
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<tr>
<td>AST (SGOT) IU/L</td>
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<td>Alkaline Phosphatase IU/L (31-126)</td>
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<td>GGT IU/L</td>
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<td>Total bilirubin mg/dl (0.1-1)</td>
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<td>7.6</td>
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<td>Direct bilirubin mg/dl (0.1-1)</td>
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<td>3.8</td>
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<tr>
<td>HDL cholesterol mg/dl (30-70)</td>
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<td>9</td>
<td>4</td>
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<tr>
<td>LDL cholesterol mg/dl (0-100)</td>
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<td>354</td>
<td>355</td>
<td>311</td>
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<td>Triglyceride mg/dl (35-200)</td>
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<td>Cholesterol mg/dl (135-200)</td>
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<td>423</td>
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<td>Testosterone ng/ml (1.7-7.4)</td>
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<td>FSH mIU/ML (1.8-9)</td>
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<tr>
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<td>1.3</td>
<td>5.1</td>
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AST= aspartate aminotransferase; SGOT= serum glutamic oxaloacetic transaminase; ALT= alanine aminotransferase; SGPT = serum glutamic pyruvate transaminase; GGT= gamma-glutamyl transferase; HDL-C= High-Density Lipoprotein Cholesterol; LDL-C=Low-Density Lipoprotein Cholesterol; FSH= Follicle-stimulating hormone; LH= Luteinizing hormone

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**APOLIPOPROTEINS**
patient despite 8 weeks’ use of AAS, the side effects were reversible and the lipid profile returned to baseline after discontinuation of AAS.

Chronic cholestatic liver disease is associated with an increased serum LDL-C and often high HDL-C. In our case, the liver biopsy showed canalicular cholestasis, but liver obstructive enzymes were only mildly elevated and the HDL-C was very low, suggesting the lipoprotein changes were due to the AAS. Although methasteron has been reported to cause cholestatic jaundice, its effect on lipid profile was not reported.

In about 60% of AAS users, decrease in libido occurs after using anabolic androgens, which is typically reversible. The exact time needed for full recovery is unknown and varies based on the dose and duration of AAS use. Full recovery may take from 4–5 months to more than a year. Testosterone levels in our patient returned to the baseline in 4 months after discontinuation of AAS.

According to a recent position statement from the Endocrine Society, the dangers of AAS, including those advertised as “designer steroids,” should be publicized. The manufacturing and distribution of all hormones and pro-hormones, including sales via the Internet, need to be regulated. Given the continuous development of so-called “designer drugs,” high quality laboratory methodologies for the measurement of these products are essential, otherwise detecting the presence of these substances would be extremely difficult.

CONCLUSIONS
AAS use may result in various adverse effects. This report demonstrates the importance of public knowledge about their potential effects, especially since these products may be advertised as nutrient supplements. The magnitude of lipoprotein changes was unique in our case.

DISCLOSURE
The authors have no conflicts of interest to disclose.

ACKNOWLEDGEMENTS
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REFERENCES
This article focuses on actual lipid disorders from actual patients, and how one clinical lipidologist evaluates the available clinical and laboratory data and then arrives at a therapeutic solution. Dr Dayspring has been in practice 33 years and lectures extensively through the country on lipids and lipoprotein disorders.

Case 1—A routine Ob/Gyn exam leads to complications:
I received the following case from a gynecologist who is quite adept at cardiovascular disease (CVD) risk recognition and management. The patient is an asymptomatic 48 year old, thin, perimenopausal, normotensive, non-smoking, Caucasian female whom was seen for a routine annual gynecological exam. Interestingly, her normal mammogram was reported as showing some arterial calcifications. She was advised to have a thorough cardiac evaluation despite the absence of any family history of premature CVD. Her lipid evaluation was:

TC = 207 mg/dL  
HDL-C = 39 mg/dL  
LDL-C = 146 mg/dL  
Triglycerides = 146 mg/dL  
VLDL-C = 29 mg/dL  
Lp(a) = 139 mg/dL

An NMR LipoProfile was also performed and the gynecologist found the results to be astounding:

Total LDL-P = 2043 nmol/L (extremely high > 95th population percentile)  
LDL size was small or Pattern B at 20.2 nm (small size is < 20.6 nm)

She was started on Crestor (rosuvastatin) 10 mg and Zetia (ezetimibe) 10 mg daily. Soon thereafter, while out with her husband, she developed chest pain and dyspnea. They went to the hospital and the EKG was abnormal, so an angiogram was done and 2 stents were placed because of 90 percent stenosis of 2 vessels. She was advised to return for re-evaluation but 6 days later the chest pain, dyspnea, and clammy skin made her return and 3 additional stents were placed. She is now doing well.

Discussion:
First let’s discuss this case as to the workup and treatment before the Acute Coronary Syndrome (ACS) occurred. At her age, and with a lack of 2 major CV risk factors, she would not have qualified for Framingham Risk Scoring (FRS) using 2001 NCEP guidelines.1 The five major coronary heart disease (CHD) risk factors are age (55 in women, 45 in men), low high-density lipoprotein cholesterol (HDL-C), cigarette smoking, family history of premature CVD, and hypertension. This patient has only the low HDL-C. Thus, the FRS would classify her as low risk, but it is well recognized that FRS can leave a lot to be desired in women.2 The low-density lipoprotein cholesterol (LDL-C) goal of therapy for low-risk patients is 160 mg/dL and therapeutic lifestyle therapies would be advised. However, an aggressive reading of the 2004 NCEP interim report could be interpreted as also having an optional goal of trying to achieve an LDL-C of 130 mg/dL in this woman.3 To achieve that goal, lifestyle would still be the preferred therapeutic option with drug therapy as a secondary strategy. The AHA women’s guidelines suggest an LDL-C of < 100 mg/dL for all women to be achieved with lifestyle and medication if the risk so dictates.4

Since CVD can present as sudden death, especially in women who often have atypical symptoms that do not suggest CHD, one may not get a second clinical opportunity. Therefore it is critical that we make correct risk assessments on the initial encounter. In today’s insulin-resistant climate, we certainly have to look way beyond the LDL-C value. So, let’s take a real close look at the lipid profile. The very low (for a woman) HDL-C of 39 mg/dL is a major risk factor. Based on the initial history, most providers would probably not have ordered lipoprotein (a), as it was deemed an emerging risk factor by NCEP ATP-III. However, it was ordered and the elevated
Lp(a) in a Caucasian woman is a risk factor if the level is very high (as in this case) and also associated with elevated LDL-C. The TC/HDL-C is 5.3 (N < 4.0). The non-HDL-C, calculated as total cholesterol (TC) minus HDL-C, is 168 mg/dL (elevated according to AHA women’s guidelines, but non-applicable in this case according to NCEP as the triglycerides (TG) are not > 200 mg/dL. Both the TC/HDL-C ratio and non HDL-C level are surrogates of elevated apoB (the potentially atherogenic lipoproteins). The TG/HDL-C ratio is 3.7, a level highly associated with predominately small LDL particles. Almost all drug naïve patients with small LDL particles have elevated apoB or LDL-P. Thus, a careful analysis of the lipid profile in this woman is certainly suggestive of too many LDL particles (high apoB) with the predominant size likely being small. Finally, although guidelines do not yet recognize breast arterial calcification as a CHD risk equivalent, there is data that it is linked to systemic atherosclerosis.

The NMR lipoprotein analysis clearly demonstrates significant worry. Using population cutpoints from studies like Framingham Offspring and MESA (Multi-Ethnic Study of Atherosclerosis), an LDL-P > 1600 nmol/L is considered high (75–80 % of patients will have lower levels) and > 2000 is very high (90% of patients have lower levels). One might think this is another case where lipoprotein quantification outperforms lipid concentrations in predicting risk, however an LDL-C of 146 mg/dL is also in the 70th–80th percentile Framingham population cutpoint. The major factors determining apoB (LDL particle) entry into the arterial intima is particle concentration and endothelial function/integrity. LDL size per se is not a major factor influencing arterial entry as all LDL particles (large or small) and even larger remnant lipoproteins, if present in elevated concentrations, can penetrate the endothelium. Putting it all together (before the acute coronary syndrome): We had a perimenopausal woman without obvious historical risk factors who had (1) a very worrisome lipid profile, (2) a terrible lipoprotein profile, (3) arterial calcium seen on mammography and who was (4) probably an insulin resistant metabolic syndrome patient (low HDL-C, TG nearly 150 mg/dL and increased numbers of small LDL particles). I believe the clinician was correct and very wise to start aggressive lipoprotein modification with lifestyle and drugs (statin and ezetimibe) in such a patient. Despite the perfect FRS, there were plenty of indicators that identified this woman as high risk.

With an LDL-P > 2000 nmol/L, the most potent statin (rosuvastatin) with ezetimibe was a good choice to get rapid lowering of apoB (atherogenic LDL particles). Multiple studies reveal that you get as much (approximately 20%) apoB reduction by adding ezetimibe to the starting dose of any statin than you do by using higher doses of the statin (and most statin side effects are dose related). The ezetimibe will also negate the usual reflexive statin-induced hyperabsorption of sterols. The high Lp(a) does not alter the choice of statin/ezetimibe therapy as NCEP suggests the proper way to reduce risk in persons with elevated Lp(a) is to normalize LDL-C.

Aspirin and blood pressure (BP) control were also clearly indicated at the time of presentation. Believing her to be high risk, I would have also prescribed omega-3 fatty acids at 1000 mg dosage as AHA/ACC recommends for high-risk patients with CHD. Unfortunately, this woman almost died due to severe coronary artery disease (CAD) and
multiple unstable plaques, and she is now a very high risk patient. Although the woman received proper treatment by her gynecologist, would any additional studies have provided clues that she was on the brink of an event or acute coronary syndrome (ACS)? The answer is probably yes and of course it is always so easy to do this with the retrospectoscope: They are: (1) If you determine someone approaching age 50 is in a high-risk category, stress testing is indicated to rule out significant obstructive disease and to determine a functional capacity so a proper exercise prescription can be advised. Had it been done, the stenotic lesions might have been discovered; (2) use of high-sensitivity C-reactive protein (hs-CRP) and/or Lipoprotein Associated Phospholipase A2 test (available as the PLAC test) might have given us a better idea regarding vascular inflammation, plaque vulnerability and imminent risk. The PLAC test is stable and more specific (unlike CRP) for vascular events (including stroke which is always a higher worry in a woman than in a man). Cost can be a consideration on which inflammatory marker to order. I am not sure that CIMT testing would have told us anything more than did the mammograms, i.e., that atherosclerosis was present.

Because she is now in the very high risk category, we must be very aggressive in normalizing the treatable risk factors.

On future follow up, what would one turn to if the rosvastatin (10–20 mg)/ezetimibe 10 mg tablet did not normalize the lipid profile or LDL-P? I believe this woman with cardiometabolic risk needs to be followed with apoB or LDL-P, as per the recent ADA/ACC consensus statement.9 Because she is now in the very high risk category, we must be very aggressive in normalizing the treatable risk factors. Here are potential options (in the order I would use them): I’d consider a therapy that shifts LDL size as it is easier for upregulated LDL receptors to recognize the apoB configuration on normal sized rather than small LDL. Since neither statins nor ezetimibe typically shift LDL size, adding extended-release niacin, a fibrate, or higher dose prescription strength Omega-3 fatty acid (FA) esters to the regimen might help and thus further lower LDL-P. If needed to get to goal, in this case where the TG were < 200 mg/dL, I’d go with extended-release niacin (Niaspan). There is positive lipid-modulating data using statin/ezetimibe/extended-release niacin.10 In the HDL Atherosclerosis Study (HATS) study, slow-niacin (and additional IR niacin in some) added to a statin in high-risk patients demonstrated dramatic angiographic and very positive outcome data. There is little niacin outcome data in women, and a perimenopausal woman is likely to be already dealing with vasomotor symptoms which might limit its use. Many might consider niacin an especially good choice because of the elevated Lp(a) and low HDL-C. However, there are no prospective trials showing reducing apoprotein (a) levels with any drug improves outcomes. There were some interesting potential positive effects of estrogen in Heart and Estrogen/progestin Replacement Study (HERS) in women with elevated Lp(a).11

Case 2—Diabetes presents a challenge:
The case discusses a frequent dilemma: Do all diabetic patients need statins? I was asked about a 42-year-old male who presented with a diagnosis of Type 2 diabetes mellitus (T2DM), solitary kidney, hypertension (controlled with verapamil 240 mg daily and valsartan [Diovan] 160 mg daily) and with a history of biopsy diagnosed NASH (nonalcoholic steatotic hepatitis) as well as microalbuminuria.

**Initial lipid panel:**
- TC = 189 mg/dL
- TG = 477 mg/dL
- HDL-C = 30 mg/dL
- LDL-C = 64 mg/dL
- VLDL-C = 95 mg/dL
- non-HDL-C = 159 mg/dL
- TC/HDL-C = 6.3
- TG/HDL-C = 15.9

The provider started metformin with eventual titration to 1000 mg twice a day, ASA 81 mg daily and simvastatin/ezetimibe (Vytorin) 20/10. The very next day, the liver function tests (LFTs) came back and were significantly elevated (ALT 176, AST 110). The clinician
discontinued Vytorin and emphasized the importance of therapeutic lifestyle and prescribed fenofibrate (TriCor) 145 mg daily, pioglitazone (Actos) 15 mg daily and Omega-3 FA 1000 mg 3–4/day. Since then the patient has lost 30 pounds and the LFTs have come down (over 12 weeks) to normal values (AST 41, ALT 51). His HgbA1c is now fine and microalbumin also returned to normal. The verapamil had to be stopped as the patient was having symptoms of pre-syncope with a systolic BP in the 90–110s.

After seeing the follow up lipid panel, the provider asks, “Can I even make an argument for prescribing a statin?”

TC = 182 mg/dL
HDL = 99 mg/dL
TG = 123 mg/dL
LDL-C = 58 mg/dL
VLDL-C = 25 mg/dL
non-HDL-C = 83
TC/HDL-C = 1.9

Discussion:
The approach and management (with one exception) seems to be a fabulous therapeutic job. The exception is that there is a major P450 interaction between simvastatin and verapamil and you really should not use them both in a polypharmacy patient (if you do, the dose of simvastatin should not exceed 20 mg). A hydrophilic statin (pravastatin or the more potent rosvastatin) would have been a safer choice. With respect to the provider’s inquiry as to whether a statin is, required, most practitioners believe diabetics must be on a statin for their lipid and so-called non-lipid or pleiotropic effects. Lipid and CV guru Michael Davidson, MD, in an editorial about statin pleiotropy reminded readers that, “The National Cholesterol Education Program Adult Treatment Panel III guidelines do not recommend specific drugs to reduce CHD events but rather lipoprotein target goals based on the weight of clinical evidence. Among clinicians the pleiotropic benefits of statins have reached almost mythical proportions. Although research and debate regarding this issue should continue, in the absence of evidence for benefits on events from randomized clinical trials, the focus must remain on achieving the recommended goals of therapy established by national guidelines.” Since then, JUPITER Trial data suggests reducing CRP levels might be important, but it is speculative that lowering CRP is necessarily a pleiotropic rather than cholesterol-lowering effect of statins. Ezetimibe, not known to have many pleiotropic effects, significantly lowers CRP on top of that caused by statin therapy, likely by further lowering cholesterol. If one studies NCEP and ADA guidelines closely, they are supportive of starting statin therapy in T2DM. Indeed, ADA guidelines advise that a T2DM > age 40 should start a statin and get LDL-C <100 mg/dL. If the person has CHD, statin therapy is advocated to reduce LDL-C < 70. NCEP 2004 addendum gives an option to start a statin in T2DM no matter what the baseline LDL-C and suggests reducing it by 30–40%. Yet both ADA and NCEP remind us that in diabetics with CHD and an unremarkable LDL-C that fibrates (gemfibrozil in VA HIT) reduce events. So is it considered the standard of care to use statins first line? Or perhaps we should better ask: Is it not the standard of care to start another drug first? In this case the LDL-C went from 64 to 58 (hardly a 30–40% drop). If the patient had an event, would one be questioned as to why no statin was prescribed?

Although there are no clinical trials providing evidence on what drugs best reduce events in people with high-risk TG values, most guidelines, especially NCEP ATP-III, suggest a fibrate as the preferred first line therapy if the TG are > 500 (this patient had 477). Although not mentioned when ATP-III was published in 2001, prescription strength N-3 FA (Lovaza) at doses of 4000 mg or higher also now have an FDA indication when TG are > 500 mg/dL.

The elevated aminases noted one day after starting statin/ezetimibe were clearly not drug related but due to the hepatic steatosis. Package inserts with statins and fibrates state not to use them in cases of unexplained aminase
elevations. Yet in a person with biopsy-proven NASH, the aminase elevation is not unexplained! There is no evidence I am aware of that statins are harmful in patients with fatty liver due to obesity. With respect to fibrates, in the FIELD study, fenofibrate caused no aminase elevations compared to placebo (indeed, the on-treatment aminase values were slightly less in the fenofibrate group). There are also small studies showing aggressive lipid management as well as thiazolidinedione use improves NASH and studies are in progress evaluating N3 FA use in steatosis. Therefore, if the physician has achieved lipid goal in this patient, does he or she really need to use a statin? The follow up lipid profile demonstrates at-goal lipid values: NCEP (uses LDL-C and Non HDL-C), ADA (uses LDL-C, TG and HDL-C) and Canadian guidelines (which use TC/HDL-C).

Statins, of course, have significant prospective and post hoc data in numerous trials of diabetic patients in primary prevention and secondary prevention settings. Those who are evidence based might note that there is no Level 1 outcome data using fenofibrate or pioglitazone or Omega-3 FA to reduce CV events in diabetics. But a close look at all fibrate trials (totaling > 11,000 diabetics) shows there is post hoc support of gemfibrozil (a fibrate) in high-risk diabetics with existing CHD and post hoc support of bezafibrate (not available in US) in metabolic syndrome patients. Fenofibrate has angiographic data in diabetics with existing CHD in the DAIS trial. FIELD suggested that fenofibrate significantly reduced the primary and secondary endpoints in diabetics without existing CHD. In both studies, as in this patient, fenofibrate also reduced microalbuminuria.

There is new outcome data on N-3 FA using results from the JELIS trial suggesting outcome benefit from EPA plus statin in Japanese patients with impaired glucose metabolism. Pioglitazone did reduce macrovascular events in complicated diabetics with CHD who were aggressively treated with multiple medications in the PROACTIVE trial (using a higher dose than this patient) and pioglitazone also has positive IVUS data. Metformin did impact on macrovascular events in obese T2DM in UKPDS and in a just-presented poster at the annual ADA meeting, in which a small retrospective analysis study revealed metformin can lower LDL-P in children with metabolic syndrome. There are very few trials using niacin where serious numbers of diabetics were enrolled. Although post hoc analysis of diabetic patients (again small numbers) using niacin in the Coronary Drug Project was suggestive of benefit, pending future outcome data you have to judge niacin on lipid/lipoprotein benefit (not outcome benefits).

Despite the normal on-treatment lipid profile, this is a high risk individual (many consider NASH to be a CHD equivalent as is the diabetes). It is a real challenge to accurately guess residual risk in such high risk patients based on lipid concentrations. Because of the known discordance between lipid concentrations and atherogenic particle numbers, I'd do an apoB or LDL-P on this man. There is data in T2DM showing that 41% of patients with an LDL-C < 70 mg/dL still have high LDL-P (> 1000nmol/L).

Lastly, how do we explain the tremendous therapeutic response in this patient? Clearly, his insulin resistance-related lipid abnormalities were very responsive to the therapies. The major lifestyle changes and the TZD and fibrate and Omega-3 FA certainly helped the NASH and the lipoproteins. Was it all lifestyle? You would have to reduce and eliminate the meds and follow closely to know for sure. I'd be in no hurry to stop anything quickly because we all know that lifestyle
changes in most patients are often short lived. It is also fascinating to try and figure out how the HDL-C changed so much (30 to 99 mg/dL) with the drugs involved. Was it a lab error? I think it was likely due to several factors including increased apoA-I and apoA-II production, hepatic lipase inhibition (shifting LDL size upwards), and the significant reduction in TG (which the meds and lifestyle helped). Without TG-rich lipoproteins, there would be significantly less CETP-induced transfer of TG from VLDL to HDL; the HDLs would stay large and very full of cholesterol.

In summary we had a high risk diabetic patient with NASH and an extreme TG/HDL-C axis disorder. I cannot argue with the clinician’s choice of therapies (except for the initial use of simvastatin). If you do believe the standard of care is that diabetics need a statin, then you should use it in conjunction with lifestyle changes. Personally, I do not think statin monotherapy would have achieved the current results. The clinician’s use of the fibrate, Omega-3 FA, TZD and metformin with ASA and high dose ARB shows he had a clear understanding of the problems—one cannot argue with the results.

[Attention readers: If you enjoy the case files of Dr. Dayspring, you can request a free subscription to his biweekly Lipidaholics Anonymous Cases newsletter by e-mailing the author at tdayspring@aol.com. Former cases are archived at www.lipidcenter.com under the “professionals” tab. – ed.]

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17. Cromwell WC, Otvos JD. Heterogeneity of Low-Density Lipoprotein Particle Number in Patients With Type 2 Diabetes Mellitus and Low-Density Lipoprotein Cholesterol <100 mg/dL. Am J Cardiol. 2006;98:1599-1602.
Residual Risk Reduction in Insulin Resistant Patients

The clinical concept of “residual risk” is commonly defined as risk for cardiovascular disease (CVD) events after the patient has been treated with a statin medication. At the IAS meetings held recently in Boston, I was struck by a more comprehensive definition, from the International Residual Risk Reduction Initiative (www.R3i.org): “The significant residual risk of macrovascular events and microvascular complications, which persists in most patients despite current standards of care, including achievement of low-density lipoprotein cholesterol (LDL-C) goal and intensive control of blood pressure and blood glucose.” Given the increasing incidence of insulin resistant syndrome (IRS) patients crowding our waiting rooms and clinics, and the fact that at least 2/3 of acute coronary events and strokes are occurring in insulin resistant patients, it is imperative that we focus on residual risk reduction in insulin resistant patients. In this Practical Pearl I will focus on reduction of lipoprotein-related residual risk. In addition, the reduction of diabetes risk through aggressive lifestyle modifications as well as the use of medications such as metformin and thiazolidinediones must also be considered in all IRS patients. While the concept of residual risk has largely focused on abnormalities of triglyceride (TG) and high-density lipoprotein cholesterol (HDLC) concentrations (TG/HDL-C axis abnormalities), we often forget what the lipoprotein-related etiology of that risk is.

In order to adequately manage lipoprotein-related residual risk, we need to properly assess the lipoprotein status of individual patients. Although some studies in lower-risk, noninsulin resistant populations have shown LDL-C to have a high correlation with LDL-Particle counts (LDL-P) in assessing CVD risk, several studies have shown the two measures to be significantly discordant. For those with insulin resistance it is clear that traditional lipid panel measurements are inadequate to assess and manage this risk. Lipid concentrations as proxies for lipoprotein risk often significantly under-represent CVD (cardiovascular disease) risk. The 2008 ADA/ACC consensus statement addresses these issues as the first truly lipoprotein-based consensus statement for insulin resistant patients, stating that “measurement of apolipoprotein B (apoB) is warranted in patients with cardiometabolic risk on pharmacologic treatment” who are in high or very high risk categories. The ACC/ADA statement calls for the use of directly measured apoB to guide adjustments in therapy and positions NMR-derived LDL-P as equally informative. Interestingly, as is noted in a more recent statement from the American Association of Clinical Chemistry (AACC), the lipoprotein (apoB) goals cited in the ACC/ADA consensus statement do not correlate as equivalents with the Framingham Offspring Study (FOS) population cut-points that would correlate with the lipid concentration goals advised by NCEP ATP III guidelines. The NCEP ATP III LDL-C goals for high risk and very high risk patients are 70 mg/dL (2nd percentile population cut-point) and 100 mg/dL (20th percentile cut-point) whereas ADA/ACC suggests apoB of 90 mg/dL (40th percentile cut-point) and 80 mg/dL (20th percentile cut-point). In their revision, the AACC paper advises consistent achievement of the 20th percentile of lipid and lipoprotein levels.

Table 1 is my attempt to improve outcomes, using both the 2nd percentile cut-point (for very high risk
patients) and FOS 20th percentile cut-point (for high risk patients). Further support for using a particle-based approach comes from the recent Best Practices Statement of the AACC: “In light of the mounting evidence, the members of this working group of the Lipoproteins and Vascular Diseases Division of the AACC believe that apoB and alternate measures of LDL particle concentration should be recognized and included in guidelines, rather than continuing to focus solely on LDL-C.” Although there is as yet no prospective clinical outcome data supporting the lowering of apoB to < 80 mg/dL, or LDL-P to < 1000 nmol/L, it is my opinion that the clinician should recognize the increased relative CVD risk of the NCEP ATP III “very high risk” category, and treat beyond the AACC Best Practices group’s recommendations to the population-based lipoprotein goals in Table 1. Examination of the Framingham Offspring epidemiologic data provides support for this concept. In this study of CVD event-free survival of over 3000 participants (mean age 51; 53% women), LDL-C was not at all associated with risk in men and only weakly associated with risk in women. Non-HDL-C provided risk prediction intermediate between LDL-P and LDL-C. However, a substantial subset (21%) of the individuals with discordant LDL-C vs. LDL-P values had higher LDL-P, and these discordant individuals had a higher CVD event rate. The corollary to this was that those individuals with a low LDL-P had a correspondingly lower CVD event rate than those with a low LDL-C. A review of 17,000 patients on LDL lowering therapy in 11 studies showed that “Many patients who achieve LDL-C and non–HDL-C target levels will not have achieved correspondingly low population-equivalent apoB or LDL-P targets. Reliance on LDL-C and non-HDL-C can create a treatment gap in which the opportunity to give maximal LDL-lowering therapy is lost.” These results suggest that at-goal apoB or LDL-P is a better indicator of reduction of residual risk than equivalently at-goal LDL-C or at-goal non-HDL-C values, and could perhaps be better utilized to manage residual LDL-related risk in IRS patients.

As of now, on-treatment clinical trial data supports the use of 2 methodologies to assess lipoprotein associated residual risk and establish therapeutic goals, non-HDL-C and apoB. Non-HDL-C is a simple calculation of apoB particle cholesterol content. Directly measured apoB is fundamentally different from non-HDL-C in that it is a measure of the number of atherogenic apoB particles. As per the AACC Best Practices group’s recommendations, “Despite a high correlation, these markers are only moderately concordant, indicating that one cannot simply substitute a marker for another in classifying patients into risk categories. Importantly, on-treatment non-HDL-C concentrations may not reflect residual risk associated with increased LDL particle number. The use of LDL particle counts by NMR is supported by epidemiologic data. All 3 of these methodologies are superior to traditional LDL-C assessment of LDL risk, especially in IRS populations, where the presence of large numbers of TG-rich lipoproteins and remnant particles, and small, dense LDL particles create a “disconnect” between the traditional parameter for assessment of LDL-related risk, LDL-C (cholesterol content), and the more accurate determinant of LDL risk, apoB or LDL-P, the number of atherogenic particles. It should be noted, however, that FOS data indicates that remnants and VLDL-P played almost no role in CVD risk beyond LDL-P, and that non-HDL-C should be viewed as a surrogate of LDL-P itself. A recent meta-analysis of multiple different techniques of lipoprotein risk assessment concluded that there was no significant advantage to assessing LDL subfractions over standard lipid determinations. However, the meta-analysis showed that in multiple studies the assessment of LDL particle number (LDL-P) was associated with CVD incidence. Perhaps surprisingly to some, LDL particle size and small LDL particle fraction were not as consistently associated with incident disease, confirming earlier analyses from the MESA study showing that once adjusted for LDL-P, LDL particle size disappears as a predictor of risk (as assessed by carotid IMT surrogate).

The second component of lipoprotein-associated residual

**If we prevent the disease, we will prevent the events and if we take away the atherogenic particles, we will take away the atherosclerosis.**
risk in insulin resistant patients is the risk beyond apoB
elevation inherent in abnormalities of HDL function and
triglyceride elevation. Even modest pre- and postprandial
elevations of TG (> 130 mg/dL fasting and > 150 mg/dL
2 hrs postprandial) are known to increase cardiovascular
risk through multiple mechanisms beyond apoB elevation,
including increases in blood viscosity, hypercoagulability,
endothelial dysfunction, and inflammation of atherogenic
plaque. Fibrates, high-dose niacin and very high dose
omega-3 fatty acids (N3FA) all help reduce
TG elevations in these patients. The elevated
TG levels seen in IRS also lead to the TG enrichment
of HDL particles and the accompanying drop in
HDL functionality and HDL particle numbers via
increased HDL catabolism. Although readily available
tools to assess HDL functionality are lacking,
we must realize that HDL-C content is inadequate to
assess HDL functionality, either in drug naïve patients or
in patients on medication. Clinical trials with the HDL-C
increasing agents fibrates and niacin are associated with
CVD event reductions, in the fibrates’ case even with
only modest increases in HDL-C in VA-HIT and HHS, and
a negligible increase in FIELD. Fibrates and niacin (as well
as ezetimibe and colesevelam) improve HDL functionality
by increasing the critical step of macrophage reverse
cholesterol transport. Niacin shifts in HDL subpopulations
correlated with angiographic disease reduction in the
HATS trial, and gemfibrozil shifts in HDL-P (HDL particle
count) and HDL subfractions predicted new CHD events
in VA-HIT. Gemfibrozil induced HDL subpopulation
changes in LOCAT predicted angiographic progression of
disease and similar results were found with bezafibrate
in BECAIT. Fibrates and niacin beneficially affect HDL
proteomics (the protein makeup of HDL), likely improving
HDL functionality. It is tempting to speculate that this
increased HDL functionality will be associated with
residual risk reduction. It is important to realize that even
patients with seemingly “isolated low HDL-C” physiology
TABLE 2

| Statin +/- colesevelam or ezetimibe to reduce apoB/LDL-P to desired levels. |
| Additional agents to further reduce apoB/LDL-P if needed, and to increase macrophage reverse cholesterol transport/HDL functionality, and to reduce triglyceride rich lipoproteins. |
| Fenofibrate in T2DM patients, esp. with triglycerides > 200 mg/dL and low HDL-C. |
| Niacin in secondary prevention settings. |
| Pharmacologic dose N-3FA are an alternative. |

on examination of standard lipid panels often have
significantly increased numbers of (usually small
dense) LDL particles. Such low HDL-C states in IRS
are most often simply surrogates for the presence of
a large amount of LDL-P associated risk. Evidence
from small clinical trials (HATS, FATS, AREGS, SANDS,
etc.) is beginning to accumulate that addressing the
LDL axis abnormalities and abnormalities of the HDL/
triglyceride axis with various combinations of statins,
niacin, fibrates, bile acid sequestrants and ezetimibe,
provides superior CVD risk reduction, as measured by
imaging procedures. Large scale clinical trials such as
ACCORD, AIM-HIGH and
IMPROVE-IT will provide
additional data in this
regard.

How can we best manage
residual risk in insulin-
resistant patients? (See Table
2.) By realizing that it is
essential to go beyond traditional lipid concentration-
based proxies as therapeutic goals in these patients,
we have the potential to accomplish this objective:
“If we prevent the disease, we will prevent the events
and that if we take away the atherogenic particles,
we will take away the atherosclerosis” Even the
inflammatory aspect of atherosclerosis is most likely
driven by excessive numbers of atherogenic particles.
Our top priority must then be to reduce atherogenic
particle numbers by reducing their formation or
enhancing their clearance by upregulating LDL
receptors with agents such as statins, ezetimibe and
colesevelam, and then to monitor the efficacy of these
agents with achievement of a low risk (low LDL-P)
state. The effort to reduce atherogenic particles is
of course a partnership between the clinician and
patient: the patient can likely decrease LDL particle
production (through therapeutic lifestyle changes)
at least as much as the clinician can increase LDL
clearance (through pharmacologic intervention). We
need to reduce the risk of TG-rich lipoproteins
continued on page 25
Treatment Induced HDL-C Change Is Not Associated with Cardiovascular Benefit in Meta-regression Analysis

Though the benefits of statin therapy are robust, considerable residual cardiovascular disease (CVD) risk remains in many patients. This has stimulated interest in other lipid-modifying treatments such as high-density lipoprotein cholesterol (HDL-C) raising. The National Cholesterol Education Program Adult Treatment Panel III in 2001 confirmed that an HDL-C level <40 mg/dL is a major risk factor and has suggested that once low-density lipoprotein cholesterol (LDL-C) and non-HDL-C levels are lowered to targets in subjects with high risk, that niacin or fibrate therapy may be considered as additional therapy. No targets were set for HDL-C raising because of the absence of sufficient clinical trial evidence to support the concept of a therapeutic HDL-C target. Several trials with niacin or fibrate therapy have shown clinical benefit, although it is unclear whether this is related to changes in HDL-C. In addition a clinical trial with torcetrapib, an agent that significantly increased HDL-C, was accompanied by increased mortality, although it is uncertain whether this finding was related to an off-target action of the drug to raise blood pressure.

In an effort to examine whether a relationship exists between changes in HDL-C in controlled clinical trials and cardiovascular disease (CVD), a recent meta-analysis of all valid, controlled clinical trials was recently undertaken. The authors included all randomized clinical trials that compared any lipid-modifying agent or diet with placebo or usual care, or compared a more intensive with a less intensive lipid-modifying treatment. After careful evaluation, a total of 108 trials were included for analysis; these included trials using statins (n=54); fibrates (9); resins (3); niacin combinations with a statin, fibrate, or resin (6); n-3 fatty acids (9); acyl-CoA:cholesterol acyltransferase inhibitors (2); probucol (2); glitazones (2); hormones (9); torcetrapib (2); and low fat diets and surgery (5). In total, 146,890 participants were included in the intervention groups and 152,420 in the control groups. The weighted mean baseline LDL-C concentration of all participants was 140 (SD 23; range 84–279) mg/dL, and the HDL-C concentration was 47 (SD 7.4; 32–62) mg/dL. The mean change in LDL-C was -23 (SD 19) mg/dL and in HDL-C was 1.7 (SD 3.1) mg/dL. The change in LDL-C was found to be associated with the risk of CVD in multivariable meta-regression analysis adjusted for change in HDL-C and different drug classes, as has been well documented before. The risk ratio for coronary heart disease events (death or non-fatal myocardial infarction) was reduced on average by 7.1% (p <0.001) per 10 mg/dL reduction in LDL-C. By contrast, no significant association of change in HDL-C with the risk ratio after adjustment for changes in LDL-C was found. Prespecified analyses focusing on a more homogeneous sample of trials using interventions known to raise HDL-C and excluding trials using agents associated with harmful effects did reveal a significant association of change in HDL-C with the risk ratio for coronary heart disease events in univariable analysis, (29% risk reduction for each 10 mg/dL increase in HDL-C; p <0.01). However, this association was no longer detectable after changes in LDL-C were taken into account.

Thus in these trials the apparent reduction in outcomes was due to the association of changes in HDL-C with changes in LDL-C.

What to make of these negative findings? Meta-analyses do not carry the power of randomized clinical trials and are essentially observational studies that compare trials with many different agents that affect HDL in varying ways, producing a range of changes in HDL-C. Furthermore, the mean increase in HDL-C was only ~5% which may have limited the ability to show any effect. Nevertheless, this is...
The Accreditation Council for Clinical Lipidology (ACCL) is an independent certifying organization that has developed standards and an examination in the field of Clinical Lipidology for the growing number of allied health professionals who manage and treat patients with lipid and other related disorders.

The ACCL offers two unique pathways to certification and competency assessment in Clinical Lipidology:

- The Certified Lipid Specialist program is an advanced certification pathway open to licensed Allied Health Professionals specializing in lipid management.
- The Basic Competency in Clinical Lipidology program offers a competency assessment and credentialing pathway for any healthcare professional or paraprofessional with an interest or involvement in the area of dyslipidemia.

Each pathway offers a unique application process and examination that will assess and validate the specialized knowledge and training required to practice or work in the multifaceted and unique field of lipidology. Both exams are offered electronically at testing center locations around the country for maximum convenience and cost-effectiveness.

Certification and credentialing by the ACCL demonstrates your professional commitment to the prevention of cardiovascular disease and documents your expertise in lipid management for patients, referring professionals, employers and colleagues.

Need more information about ACCL exams? Learn about the exams, the prerequisites, testing center locations, fees and topics covered in each exam. Apply online or download an application for both exams at www.lipidspecialist.org.

For additional information, please email tmackowiak@lipidspecialist.org or contact us at (904) 309-6250.

www.lipidspecialist.org
Association News

NLA Community Launches

By the time you read this, you will be able to access a new resource from the NLA—the NLA Community. This homepage is your gateway to a multifaceted social networking website developed for NLA members. All the resources of lipid.org are still available, but the new NLA Community section puts a new world of information and possibilities at your fingertips. You are invited to explore and search through the website and examine the new tools and utilities available to you. It is now much easier to find and communicate with your colleagues, and you can join and establish groups based on your particular areas of interest and expertise. Follow NLA thought leaders on their blogs—and start one of your own to share with the membership.

The NLA Community is an ongoing Scientific Forum based in your field. Like other sites with widgets, the NLA Community homepage can be tailored to reflect your interests. Select the resources and tools that suit your needs, and choose among more as we add them. Visit www.lipid.org to see what we have in store for the future of your association and clinical lipidology.

Pacific Lipid Association Leads Push to Retain Lovaza in Idaho BC/BS Formulary

Earlier this year, the Pacific Lipid Association (PLA) was informed that BlueCross/BlueShield of Idaho had elected to drop reimbursement of prescription omega-3 fatty acids (i.e., Lovaza) from its formulary in favor of over-the-counter omega-3 preparations. The leadership of the PLA drafted and sent a formal letter of advisement to BlueCross/BlueShield, strongly recommending that Lovaza be reinstated as a reimbursable treatment for high triglycerides. Chief among their concerns is the fact that prescription omega-3 fatty acids are purified and their concentration is tested and demonstrated to be effective in lowering triglycerides. Over-the-counter alternatives are an unknown quantity regarding concentration and potential inclusion of unwanted by-products. Recently we received a reply from the medical director of BlueCross/BlueShield of Idaho, in which our objections were overruled. The NLA intends to pursue this matter further and is now gathering data to be used in an appeal. If and when we call for a campaign for members to write BlueCross/BlueShield of Idaho, we hope that we can count on your support. We'll keep you posted on developments.

Deadline for Red Flag Rules Has Been Extended

Although the deadline for implementation of Red Flag Rules was originally to be August 1, 2009, we have received an extension to November 1, 2009, giving practices more time to comply with the federal directives. Briefly, this new regulation requires physicians who maintain billing accounts for patients to have written policies and procedures for identifying potential cases of identity theft and similar kinds of identity fraud. If your office is already HIPAA compliant, you will already have a framework in place to quickly implement Red Flag Rules requirements. We have an overview for you to use as a checklist available at www.lipid.org/redflagrules.

Carl J. Rubenstein, MD, Named SWLA President

Carl J. Rubenstein, MD, FNLA, was elected to serve as President of the Southwest Lipid Association (SWLA) at the Association’s 2009 Annual Scientific Forum held in Oklahoma City, Oklahoma, July 24–26, 2009. A chapter of the National Lipid Association, SWLA is a medical education society for healthcare professionals who work in the area of lipid management and preventive cardiology.

Currently serving as Clinical Professor of Medicine at the University of Oklahoma, Dr. Rubenstein is a partner in the Oklahoma Cardiovascular Associates group and Director of its Lipid-Atherosclerosis-Metabolic Program, and is on the Senior Staff of the Oklahoma Heart Hospital and Mercy Hospital. He joined the full time Cardiology faculty and the Oklahoma Medical Research Foundation in 1972, and switched to private practice in 1983. He obtained his undergraduate degree from Princeton University and earned his MD from Duke University Medical School where he also did his training in Internal Medicine and Cardiology. He has been and continues to be involved in numerous clinical research studies. He is expected to bring his considerable talents to bear on helping the Southwest Lipid Association achieve its goals in the upcoming year of his tenure as president.

Professional Development and Certification

Self-Assessment Modules Now Available Online

The Complex Lipid Management Self-Assessment Programs and NLA Self-Study Modules are part of a series of educational tools sponsored by the NLA that help to strengthen and reinforce knowledge of dyslipidemia management. While these have been traditionally offered in print format, they are now being made available for online study, with each program offering CME and CE credit.

The modules available are:

- Clinical Applications of Advanced Lipoprotein Testing, Inflammatory Markers and Non-invasive Assessments of Atherosclerosis,
- Management of Low HDL-C
From the NLA Office

• Pharmacology and Safety of Lipid-Altering Therapies
• Primary Care Series: Management of Dyslipidemia—Focus on Combination Therapies.

The CLM-SAP Online Modules can be completed at any time online, and you can return to complete a module where you left off. You can view your personal performance summary, and compare your score to that of your peers. You can even simulate an exam experience, in addition to other features offered by the online format. Learn more about these programs at www.lipid.org/education/online.

Virtual Lipid Clinic Launches on Lipid.org
In response to member requests for more case-based programming and performance improvement modules, the NLA recently launched a new educational format, the NLA vClinic™, on lipid.org. With the NLA vClinic, you’ll have the opportunity work up and manage virtual patients over multiple visits with input from leading clinical experts while earning CME/CE credit. Be sure to use the vClinic CMECompanion that accompanies these activities to assess your clinical mastery and compare your performance with other learners. Visit www.lipid.org/vclinic to participate.

Lipid Insights Virtual Journal Club
Did you know that the NLA offers perspective on clinical trials affecting clinical Lipidology through its Lipid Insights webcasts? If you miss the one of the bimonthly live Webcasts, the broadcasts are archived and offered for CME credit at www.nlacme.com.

Midwest Lipid Association Scientific Forum to Be Held September 25-27, 2009
Make plans now to attend the last NLA scientific meeting of 2009 – the MWLA Scientific Forum being held in Cincinnati, Ohio. This two-day CME/CE conference will focus on Lipid Management—From Theory to Daily Practice and is designed to help you bridge the gap from trials and research to achieving best results with your own patients. For more details see pg. 26 or register online at www.lipid.org.

Three Scientific Meetings in 2010
Please make a note that next year the NLA will be holding three scientific meetings instead of five. We have consolidated meetings by having regional chapters pair up to co-host a Winter/Spring Update and Summer/Fall Update in addition to the NLA Annual Scientific Sessions to be held in May. As always, the NLA will offer its array of professional development courses and symposia in conjunction with these 3 conferences (such as the Masters in Lipidology Course). Please see the Meetings Calendar on pg. 21 for the dates and locations. We expect increased attendance and more robust programs as a result and hope that you will plan to attend both the Annual Sessions and your region’s Scientific Forum.

4th Annual NLA Summit Conference at AHA in November
It has become a tradition for the NLA to host a scientific symposium at the American Heart Association’s Annual Meeting, and this year is no exception. This year we are co-sponsoring, together with the American Society for Preventive Cardiology (ASPC) and MedscapeCME a special 3-hour summit conference scheduled for Saturday, November 14, 2009, 8:30 am–Noon. The symposium is titled Overcoming Challenges in CVD Prevention: A Focus on the Cardiometabolic Risk Continuum and will provide a forum for experts in clinical lipidology and CVD prevention to focus on practical ways to improve how they manage their patients with dyslipidemia and cardiometabolic disorders. The sessions will be recorded for distribution as online CME modules posted on theheart.org and Medscape Cardiology. To view the agenda and register go to www.lipid.org/masterssummit.

ACCL Offers New Certification Pathway: Basic Competency in Clinical Lipidology
The Accreditation Council for Clinical Lipidology (ACCL) has developed a new competency assessment and credentialing pathway for healthcare professionals and paraprofessionals who are involved in the area of dyslipidemia. This program is designed for those who wish to demonstrate a core competency in lipid management but who do not meet the eligibility criteria required to sit for the Clinical Lipid Specialist exam offered by the ACCL (open to only licensed allied health professionals) or the physician board exam offered through the American Board of Clinical Lipidology.

Applicants for the Basic Competency in Clinical Lipidology (BCCL) exam will need to have completed a minimum of 10 CE credit hours in clinical lipidology and these can be obtained in several ways, such as by completing the NLA Lipid Management Training Course, the first volume of the NLA-SAP, or by taking the NLA Masters in Lipidology Course. The BCCL exam is offered electronically in testing centers throughout the US and Canada. To learn more about the exam and qualification criteria, visit www.lipidspecialist.org.

ABCL Physician Certifying Exam Goes Online
The American Board of Clinical Lipidology has announced that starting in 2010 the physician certifying examination will be offered electronically in proctored testing centers across the US and Canada. There will be three 30-day testing windows in the spring, summer and fall offering candidates more accessibility to the exam while minimizing costs. Go to the ABCL website at www.lipidboard.org for details.

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NLA Members — Your Medicare Incentive Check Is Waiting.

Go to nla.pqriwizard.com and learn how to earn up to 2% bonus of Medicare allowed charges.

The PQRIwizard offers NLA members a simple and cost-effective online tool to collect and report quality measure data under the CMS PQRI 2009 incentive program. This year, the incentive program is paying eligible professionals a 2% bonus on allowed charges for successfully reporting quality measures.

How Does it Work?
• It’s a simple step-by-step approach—like online tax preparation software
• No codes required—just answer a few questions per patient
• The Wizard checks for missing data to validate your report
• Once validated, the Wizard submits the results to CMS for payment

What’s the Benefit?
• Improve patient care through evidence-based measures based on clinical guidelines
• Prepare for future pay-for-performance programs
• Earn a 2% bonus on allowed charges

What’s the Cost?
There is a $299 fee for registration. If you bill CMS frequently, you will soon recoup the cost.

Who Can Participate?
For NLA members, the list of eligible professionals include:
• Doctor of Medicine
• Doctor of Osteopathy
• Physician Assistant
• Nurse Practitioner
• Clinical Nurse Specialist
• Clinical Social Worker
• Registered Dietician
• Nutrition Professional

For a full list of eligible professionals, go to www.nla.pqriwizard.com and click on “Eligible Professionals.”

What Measure Groups are Relevant to NLA Members?
Measure groups are created for specific conditions that are addressed by at least four measures that share a common denominator specification. Diabetes Mellitus is the PQRI measure group applicable for NLA members. Measures include:
• Hemoglobin A1c Poor Control in Type 1 or 2 Diabetes Mellitus
• Low Density Lipoprotein Control in Type 1 or 2 Diabetes Mellitus
• High Blood Pressure Control in Type 1 or 2 Diabetes Mellitus
• Dilated Eye Exam in Diabetic Patient
• Urine Screening for Microalbumin or Medical Attention for Nephropathy in Diabetic Patients
• Foot Exam

To register or learn more, go to nla.pqriwizard.com
2009–2010 Events Calendar

Online Activities
Available at www.nlacme.com

Webcast: October 2008–October 2009
Webcast: NLA Cardiometabolic Risk Reduction Online Case Studies
Sponsored by the NLA

Webcast: April 2009–April 2010
The Strong Heart Study and SANDS: From observation to intervention
Sponsored by the NLA

Webcast: July 2009–July 2010
Should an LDL-C less than 70 mg/dL and a CRP less than 2 mg/L be dual targets of therapy? Pro and Con
Sponsored by the NLA

Online Self-assessment Programs
4 Complex Lipid Management SAPs are available:
Ed. 11: Clinical Applications of Advanced Lipoprotein Testing, Inflammatory Markers and Non-invasive Assessments of Atherosclerosis
Ed. 12: Management of Low HDL-C
Ed. 1: Management of Dyslipidemia—Focus on Combination Therapies
Ed. 2: Pharmacology and Safety of Lipid-Altering Therapies

These programs are available online at: www.lipid.org/education/online

2009 Meetings & Courses

September 25–27, 2009
MWLA 6th Annual Scientific Forum
Cincinnati, OH
www.lipid.org

October 7–10, 2009
The Cardiometabolic Health Congress (CMHC)
Boston, MA
www.cardiometabolichealth.org

October 24, 2009
1st Annual Orange County Symposium on Cardiovascular Disease Prevention through Clinical Lipidology: A Primer with Contemporary Issues
Anaheim, CA
Sponsored by the NLA
www.lipid.org/ocsymposium
E-mail: elingerfelt@lipid.org

November 5–7, 2009
7th Annual World Congress on the Insulin Resistance Syndrome
San Francisco, CA (NLA members receive 25% off registration)
Endorsed by the NLA
www.insulinresistance.us

November 14, 2009
4th Annual NLA Masters Summit at AHA: Overcoming Challenges in Preventing Cardiovascular Disease—A Focus on the Cardiometabolic Risk Continuum
Orlando, FL
Sponsored by the NLA
www.lipid.org/masterssummit

November 14–18, 2009
American Heart Association Scientific Sessions
Orlando, FL
scientificsessions.americanheart.org

2010 Meetings & Courses

February 19–21, 2010
NLA Regional Forum—Winter/Spring
(held by the Pacific and Southwest Regional Chapters)
The Palace Hotel
San Francisco, CA

May 13–16, 2010
NLA 2010 Annual Scientific Sessions
(held by the Midwest Regional Chapter)
Sheraton Hotel and Towers
Chicago, IL

August 27–29, 2010
NLA Regional Forum—Summer/Fall
(held by the Southeast and Northeast Regional Chapters)
The Mayflower Hotel
Washington, DC

NLA Professional Development Courses

February 18–19, 2010
• Lipid Management Training Course
• Masters in Lipidology Course
The Palace Hotel
San Francisco, CA

May 12–13, 2010
• Lipid Management Training Course
• Masters in Lipidology Course
Sheraton Hotel and Towers
Chicago, IL

August 26–27, 2010
• Lipid Management Training Course
• Masters in Lipidology Course
Mayflower Hotel
Washington, DC
Email: lwotto@lipid.org
Lipidology Outreach, Grants and Public Health

The new Foundation of the NLA (FNLA) is already beginning to receive grant applications, but there are funds still available for viable programs or research projects. The Foundation was created in late 2008 to serve as the charitable arm of the National Lipid Association and promote education and research with an emphasis on serving professional, community and public health interests.

The Foundation is currently accepting applications for grants in the following areas:
- Research
- Medical Education
- Community Outreach

A good example of the type of grants the Foundation is funding is the First Annual Orange County Symposium: Cardiovascular Disease Protection Through Clinical Lipidology: A Primer with Contemporary Issues. Program Co-chair Paul Rosenblit, MD, applied for a Medical Education Grant and received $5,000 from the Foundation to help fund the symposium. The program is jointly sponsored by the NLA, the Pacific Lipid Association, the American Society for Preventive Cardiology and the California Chapter of the American College of Cardiology.

Support Your Foundation
Replenishing the funds for the Foundation's grant program is essential to ensure the future viability and health of our organization. You can help by donating. Take a moment now to invest in the future of your Foundation. Your donation will help support professional outreach and education and promote public awareness of critical issues in public health.

Three easy ways to donate to the FNLA:
- Log onto www.lipidfoundation.org and click on “Donate”
- Call 904.309.6260 and ask for Cindy Moore
- Mail your donation to Foundation of the NLA 6816 Southpoint Parkway, Suite 1000 Jacksonville, FL 32216

Industry Donation Challenge
The Foundation and NLA Board has issued a challenge to industry supporters to match the NLA’s donation to the Foundation in the amount of $125,000. Reach out to your contacts and ask them to support the education and community outreach mission of the FNLA by providing a matching donation. To learn more about this grant challenge, please call Karen Kent at 904.309.6211.

The Online Application Process
An online Grant Application Form and complete instructions can be found at www.lipidfoundation.org. When applying for a grant, either create a grant system account (if this is your first time applying) or login to your existing grant system account as appropriate. A single account can apply for and manage multiple grant submissions, so you won’t need a new account for each grant application you submit. After registering, you can save your online grant applications and complete them at your convenience. Also, you can check on the status of your pending applications at any time.

Note that completed applications, including all supporting documentation, must be submitted at least 60 business days prior to the date you need to receive a funding decision regarding your grant application. Each application is given careful consideration as part of a rigorous evaluation by the Foundation Grants Review Committee. As a result, it may take up to three weeks for you to receive a decision regarding your application. Once approved, grant payments will be made within two weeks.
Visit the NLA vClinic to experience the latest in cutting-edge CME and lipid-focused education.

You’ll meet with “virtual patients,” make assessments, and manage them over time across multiple visits. Make decisions and see outcomes. Compare your ideas against those of your peers and consult with leading clinical experts on best practices.

The NLA vClinic is a personalized environment that presents new patients and visits to each learner. Through this unique knowledge management platform, you can track your progress and assess your areas of strength and identify areas in which your knowledge of lipidology needs review. This kind of tailored learning is truly state-of-the-art and will adapt to your input the more you participate.

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Visit the NLA vClinic today

www.lipid.org/vclinic

Treat and manage virtual patients that mirror your clinical practice and earn CME/CE credit

Instantly get expert feedback on your management decisions

Discuss management issues with colleagues

Benchmark your performance with peers

To apply online or learn more, log onto www.lipidfoundation.org and click on “Grants.” If you have any questions, please call Karen Kent at 904.309.6211.
This year, we will also provide online lipid education specifically geared toward cardiology fellows in training. Fellows will be provided access through their training program to a 50 question version of the NLA-SAP with pre-test, question critiques, and post-test. This activity will be ideal for incorporation into fellow learning portfolios and will provide important outcomes data for individual programs benchmarked to the aggregate data from all participating programs. The program is strongly supported by the American College of Cardiology CV Training and Workforce Committee and is slated to go live on 9/1/09. Be sure to ask your Program Director about this.

**Transparency and Conflict of Interest**

Transparency is an absolute must for any organization in the current era. The NLA has been proactive by posting disclosures for all NLA Board members on the NLA website and our funding sources are published in our public tax return statements as required by law. Beginning with this year, the NLA will also publish honoraria paid to individual NLA members for such NLA activities as lectures, curricular development, task force participation etc. Chris Seymour and his team will continue to work very hard to provide these data accurately and in a timely fashion. But we need your help: the disclosure data posted on the website are only as good as the data you provide. Please update your disclosures regularly and provide comprehensive listings of any activities that could be perceived as a potential conflict of interest. During board meetings, leadership conference calls etc. it is absolutely critical that you make everybody aware of any potential conflicts of interest related to the topic under discussion and that you recuse yourself from voting on these topics. Industry has traditionally been a strong supporter of physician education and we believe that it is very important that we continue to work with our industry partners in a constructive and transparent fashion. We will appoint a Task Force that will be charged with ongoing review of NLA transparency and COI procedures in this rapidly changing national environment.

**Lipid Luminations cont. from page 16**

the largest such analysis undertaken and the negative findings point to several important corollaries. First, the CVD benefit of drugs such as niacin or gemfibrozil may not be attributable to their effects on HDL-C, nor was there any evidence that the effects of statins on HDL-C added to their beneficial effects. Second, even if the effects of these agents on HDL-C are relevant for CVD outcomes, the mechanisms by which they influence HDL metabolism vary significantly, and this needs to be better understood. Third, and expanding from the last point, what may matter more than an increase in HDL-C is whether the reverse cholesterol transport, anti-inflammatory, anti-oxidative, and antithrombotic properties of HDL thought to be important in its atheroprotective action, are enhanced by therapeutic interventions. It is likely ultimately, that this approach will turn out to be the most fruitful approach for enhancing CVD protection via the HDL mechanism.

**Reference:**

and improve HDL functionality by combining fibrates, niacin, and N3FA with the aforementioned LDL-receptor upregulating agents. Although NCEP ATP III encourages reducing TG and increasing HDL-C, there are no specific lipid goals for HDL-C or TG provided by clinical trial data at this time. Fibrates have an impressive body of evidence-based medicine for event reduction of macrovascular disease in IRS patients (with triglycerides > 200 mg/dL and low HDL-C). The microvascular event reduction of peripheral amputations, retinopathy and nephropathy in FIELD by fenofibrate makes this a reasonable choice for addition to a statin for TG/HDL axis manipulation in T2DM patients. Niacin's most impressive data is in the secondary reduction of CVD, and it should be utilized in this population. Pharmacologic dose of N3FAs have been shown to reduce CVD risk, and the latest data from the JELIS trial shows reduction of CVD events to be superior in the “impaired glucose metabolism” patients receiving the N3FA/statin combination in that trial.¹⁸

Notes:
Colescevelam may increase triglycerides, especially when baseline triglycerides are elevated. The above algorithm is my own personal attempt to improve risk reduction beyond the NCEP ATP III guidelines and thus is not consistent with those guidelines, nor does it represent the views of the NLA or Lipid Spin.

References:
1. Plutzky J. A Cardiologist’s Perspective on Cardiometabolic Risk. Am J Cardiol. 2007;100(suppl):3P-6P
4. Ibid.
Lipid Management
From Theory to Daily Practice

A Regional Scientific Forum Presented by the Midwest Lipid Association

Conference Highlights:
- Key Measurements and Biomarkers in CHD Risk Assessment
- Protective Value of Omega-3 and Omega-6 Fatty Acids
- Successful Behavioral Modification Strategies
- New Targets in Hypertension and Diabetes

Featured Ancillary Courses:
- Comprehensive Cardiometabolic Risk Reduction Course
- Masters in Lipidology Advanced Training and Board Review Course
- Lipid Management Training Course

Featured Speakers:
Louis J. Aronne, MD
New York, NY
Christie M. Ballantyne, MD
Houston, TX
Vera A. Bittner, MD
Birmingham, AL
Michael H. Davidson, MD
Chicago, IL
Tara Lynn Dall, MD
Oconomowoc, WI
William S. Harris, PhD
Sioux Falls, SD
Peter H Jones, MD
Houston, TX
Richard H. Karas, MD, PhD
Boston, MA
Kevin C. Maki, PhD
Glen Ellyn, IL
Theodore Mazzone, MD
Chicago, IL
Michael Miller, MD
Baltimore, MD
Richard M. Moe, MD, PhD
Kansas City, MO
Michael A. Moore, MD
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Jennifer G. Robinson, MD, MPH
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Overlooking historic Fountain Square, The Westin Cincinnati boasts a convenient and central downtown location. It is a leisurely outdoor stroll away from the National Underground Railroad Freedom Center, Paul Brown Stadium, US Bank Arena, the Aronoff Center for the Performing Arts, and the Contemporary Arts Center.

Register now at lipid.org/mwla

The Midwest Lipid Association is a Chapter of the National Lipid Association
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A Regional Scientific Forum Presented by the Midwest Lipid Association

Lipid Management to Daily Practice From Theory

Mail To:
NLA
6816 Southpoint Parkway, Suite 1000
Jacksonville, FL 32216

Fax to:
NLA at 904-998-0855
Fax with credit card number and signature

Online:
www.lipid.org

**Important Information**
*Master’s Course*
To purchase related study materials or the NLA-SAP’s go to:
www.lipid.org/education/nlasap.

Registration: Registration and payment must be received no later than September 11, 2009. After this date a syllabus and name badge cannot be guaranteed - so register TODAY!

Cancellation: Telephone Cancellations will not be accepted. A written notice of cancellation must be received no later than September 11, 2009. Includes Social Events and Guest Fees.

Special needs:

ADA Compliance:
Attendees who need additional reasonable accommodations or who have special needs should contact the NLA at 904-998-0854.
Ralph LaForge wants to hear your thoughts on the role of physical activity in metabolic disease.


- I would like to know reader’s thoughts on the argument that physical activity mechanisms (not withstanding heritable mechanisms) may in many cases supercede obesity as a lead causative player in metabolic disease...

Dr. Michael Davidson’s blog invites you to comment on the HALTS Trial (ARBITER 6)

What do you think the HALTS trial (ARBITER 6) will show?

Dr. Kris-Etherton shares her list of tools on the Web for patient education.

There is an ongoing need for patient education material... The websites below provide comprehensive information and tools for your patients to learn...

Look for our Daily Tips and Tutorials at lipid.org or contact one of our staff members. The NLA Community is intuitively easy to use and we want you to get the most out of your membership.

Log in now and join the conversation going on at NLA Community!